## REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated July 22, 2005 are respectfully requested.

I. Amendments

Non-elected claims 20-44 and 46 stand canceled.

Claim 2-9 stand canceled.

Claim 1 is amended to recite that R is $-(CH_2)_2$-O-$CH_2CH_3$. Support for this amendment can be found in original claim 6.

No new matter is added by way of these amendments.

II. Restriction Requirement

Applicants hereby affirm the election of Group I, claims 1-19 and 45, without traverse. Non-elected claims 20-44 and 46 stand canceled.

Applicants reserve the right to file divisional applications directed to the non-elected claims of Group II.

III. Rejections under 35 U.S.C. §112, second paragraph

Claims 10-19 and 45 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

With regard to claim 10, Applicants have amended the claim in accord with the Examiner's kind suggestion

With regard to claim 45, the Examiner is respectfully directed to page 23, line 19 through page 24, line 10, where conditions responsive to treatment by rapamycin are described including wound healing, transplant rejection, neoplastic diseases, and vascular injury or inflammatory conditions such as atherosclerosis and restenosis, . Applicants further submit that conditions "responsive to treatment by rapamycin" are well known to those skilled in the art. For Example, the MedlinePlus database (http://www.nlm.nih.gov/medlineplus/druginfo/medmaster.html) lists

indications for sirolimus (rapamycin). Further, a search of the Pubmed database (http://www.ncbi.nlm.nih.gov/entrez/) using either sirolimus or rapamycin and treatment resulted in 2636 entries. Thus, the language "responsive to treatment by rapamycin" is clear to those skilled in the art based on the teaching in the specification as well as the knowledge of those skilled in the art.

In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

IV. Rejection under 35 U.S.C. §102

Claims 1 and 7-10 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Caufield *et al.* (U.S. Patent No. 5,151,143).

Claims 1-5 and 7-9 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Cottens *et al.* (U.S. Patent No. 5,912,253).

Claims 1 and 7-9 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Cottens *et al.* (U.S. Patent No. 5,378,836).

These rejections are respectfully traversed.

A. The Present Invention

Claim 1, as amended, relates to a 42-O-ethoxyethyl rapamycin compound (claim 1). Claim 10 relates to a pharmaceutical composition comprising the 42-O-ethoxyethyl rapamycin compound.

B. The Cited Art

CAUFIELD ET AL. relate to derivatives of rapamycin where the hydroxyl group at positions 31 and/or 42 are reacted with acetal forming reagents.

COTTENS ET AL. describe to demethoxy derivatives of rapamycin.

KAO ET AL. relate to oxime and hydrazone derivatives of rapamycin. Kao *et al.* disclose, as an intermediate, 42-O-(1-ethoxy-ethyl)-rapamycin.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

1. Rejection over Caufield *et al.*

Caufield *et al.* fail to show or suggest an alkoxyalkyl rapamycin derivative, or specifically a 42-O-ethoxyethyl rapamycin, as presently claimed.

With regard to claim 1, the Examiner points to the embodiment of Caufield *et al.* where the 42-O is derivatized with $-C(CH_3)_2YX$, where Y is O and X is $CH_3$. However, this structure is a branched structure in contrast to the the compound of the present invention, which is an unbranched 42-O-ethoxyethyl rapamycin.

2. Rejection over Cottens *et al.*

In Example 8, Cottens *et al.* disclose an intermediate compound of 40-O-(2-methoxyethyl)-rapamycin. However, Cottens *et al.* fail to make any mention of the specific 42-O-ethoxyethyl rapamycin compound as claimed.

3. Rejection over Kao *et al.*

Example 15 of Kao *et al.* discloses a 42-O-(1-ethoxy-ethyl)-rapamycin as an intermediate. This is a branched structure unlike the unbranched 42-O-ethoxyethyl rapamycin as presently claimed.

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met and withdrawal of the rejections under 35 U.S.C. § 102(b) is respectfully requested.

V. Rejections under 35 U.S.C. §103

Claims 1-10 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Yang *et al.* (PCT Publication No. WO 01/14387).

Applicants respectfully traverse these rejections.

A. The Present Invention

The present invention is described above.

B. The Prior Art

YANG ET AL. describe 28-epirapamycin analogs including a 43-O-MOM-28-epirapamycin.

C. Analysis

The present claims are directed to a 42-O-ethoxyethyl rapamycin. Yang *et al.* fail to show or suggest such a compound or pharmaceutical composition comprising such a compound. Instead, Yang *et al.* teach a 43-O-MOM-28-epirapamycin.

Nor would one skilled in the art be motivated to modify the 43-O-MOM-28-epirapamycin as taught by Yang *et al.* along the lines of the presently claimed invention. First, one skilled in the art would not be motivated to modify the stereochemistry of the 28-epirapamycin as taught by Yang *et al.* as the stereochemistry at the 28 position is a necessary feature of Yang *et al.* The Examiner is respectfully directed to the abstract and page 2, lines 10-26.

Second, one skilled in the art would not be motivated to further modify the compound of Yang *et al.* to substitute the 43-O-methoxymethyl for a 42-O-ethoxyethyl as presently claimed. One of skill in the art would recognize the difficulties involved in synthesizing derivatives of rapamycin as additional synthetic steps are required to protect and deprotect certain positions. Further, derivatives having a shorter overall chain length and/or overall steric bulk are less likely to produce steric hindrance of binding sites. Thus, one skilled in the art would not be motivated to modify the compound of Yang *et al.* to have a longer overall chain length.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

VI. Statutory Double Patenting Rejection under 35 U.S.C. § 101

Claims 1-19 and 45 were provisionally rejected under the 35 U.S.C. § 101 as claiming the same invention as claims 1-19 and 45 of co-pending Application No. 10/987,771. Applicants will address this rejection at such time as allowable claims are found in this or the co-owned application.

## Conclusion

Applicants respectfully submit that the pending claims are in condition for immediate allowance. The undersigned invites the Examiner to call (650) 838-4410 with any questions or comments. The Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-2207 to facilitate entry and consideration of this Amendment.

Respectfully submitted,
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